

Claims (clean version encompassing amendments)

1. (once amended) A combined preparation for simultaneous, separate or sequential use as an ultrasound contrast agent, said preparation comprising:
 - i) an injectable aqueous gas dispersion; and
 - ii) a separately administrable substance or substances capable of destabilising said dispersed gas so as at least transiently to increase the size thereof.
2. A combined preparation as claimed in claim 1 wherein the dispersed gas comprises air, nitrogen, oxygen, carbon dioxide, hydrogen, an inert gas, a sulphur fluoride, selenium hexafluoride, an optionally halogenated silane, an optionally halogenated low molecular weight hydrocarbon, a ketone, an ester or a mixture of any of the foregoing.
3. A combined preparation as claimed in claim 2 wherein the dispersed gas comprises sulphur hexafluoride or a perfluorocarbon.
4. A combined preparation as claimed in claim 3 wherein said perfluorocarbon is perfluoropropane, perfluorobutane or perfluoropentane.
5. (once amended) A combined preparation as claimed in claim 1 wherein the dispersed gas is stabilised by an initially coalescence-resisting surface membrane,

a filmogenic protein, a polymer material, a non-polymeric and non-polymerisable wall-forming material or a surfactant.

6. A combined preparation as claimed in claim 5 wherein said surfactant comprises at least one phospholipid.
7. A combined preparation as claimed in claim 6 wherein at least 75% of said surfactant comprises phospholipid molecules individually bearing net overall charge.
8. A combined preparation as claimed in claim 7 wherein said charged phospholipid molecules are selected from phosphatidylserine, phosphatidylglycerol, phosphatidylinositol, phosphatidic acid and cardiolipin molecules.

B 2 10. (twice amended) A combined preparation as claimed in claim 1 wherein said administrable substance further comprises one or more destabilising substances which induce growth of the dispersed gas by flocculation, aggregation, agglomeration, coalescence, fusion or Ostwald ripening.

11. A combined preparation as claimed in claim 10 comprising one or more destabilising substances selected from inorganic salts, aliphatic alcohols, aliphatic aldehydes, aliphatic ketones, aliphatic esters, aliphatic ethers, aliphatic amides, aliphatic nitriles, carbohydrates, polyethers, polysaccharides, polyaminoacids,

polyvinylpyrrolidone, fatty alcohols, fatty acids, fatty amines, surfactants, steroids, acids, bases and hydrotropes.

12. A combined preparation as claimed in claim 11 comprising one or more destabilising substances selected from calcium chloride, magnesium chloride, ethanol, isopropanol, ethylene glycol, propylene glycol, glycerol, sorbitol, acetaldehyde, acetone, methyl formate, methyl acetate, propyl formate, ethyl acetate, ethyl methyl ether, methyl propyl ether, di-isopropyl ether, N,N-dimethylformamide, N,N-dimethylacetamide, acetonitrile, glucose, sucrose, polyethylene glycol, polypropylene glycol, polyoxyethylene-polyoxypropylene block copolymers, dextran, starches, polylysine, gelatin, cholesterol, and surface active alkyl carboxylates, alkyl sulphonates, alkyl sulphates, dialkyl sulphosuccinates, alkyl pyridinium salts, alkylammonium salts, alkyl polyethylene glycol ethers, alkyl polyethylene glycol esters and sorbitol fatty acid esters.
13. (once amended) A combined preparation as claimed in claim 1 which further includes a vasodilator drug.
14. A combined preparation as claimed in claim 13 wherein said vasodilator drug is adenosine.
15. (once amended) A combined preparation as claimed in claim 1 which further includes a therapeutic drug.

16. (once amended) A combined preparation as claimed in claim 1 which further includes contrast-enhancing moieties for an imaging modality other than ultrasound.
17. A method of generating enhanced images of a human or non-human animal subject which comprises the steps of:
 - i) injecting a physiologically acceptable aqueous medium having gas dispersed therein into the vascular system of said subject;
 - ii) before, during or after injection of said aqueous medium administering to said subject a substance or substances capable of destabilising said dispersed gas so as at least transiently to increase the size thereof; and
 - iii) generating an ultrasound image of at least a part of said subject.
18. A method as claimed in claim 17 wherein destabilising substance is administered subcutaneously, intramuscularly, intravenously or by inhalation.
19. (once amended) A method as claimed in claim 17 wherein a vasodilator drug is coadministered to the subject.
20. A method as claimed in claim 19 wherein said vasodilator drug is adenosine.

21. (once amended) Use of a contrast agent as claimed in claim 1 in ultrasound therapy.
22. Use as claimed in claim 21 wherein said therapy involves cell killing or blocking of blood flow to a site of interest.